

PTO/SB/21 (08-03)

Approved for use through 08/30/2003. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

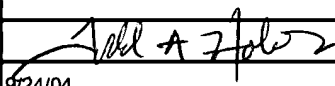
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<b>TRANSMITTAL FORM</b>  (to be used for all correspondence after initial filing)	Application Number	10/702,578	
	Filing Date	11/05/03	
	First Named Inventor	Tae-Wan Kim	
	Art Unit	1632	
	Examiner Name	to be assigned	
Total Number of Pages in This Submission	13	Attorney Docket Number	5199-14


**ENCLOSURES (Check all that apply)**

<input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input checked="" type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Response to Missing Parts/Incomplete Application <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation <input type="checkbox"/> Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____	<input type="checkbox"/> After Allowance communication to Technology Center (TC) <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): Return receipt postcard
<b>Remarks</b>		

**SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT**

Firm or Individual name	Todd Holmbo, Reg. No. 42,665
Signature	
Date	9/24/04

**CERTIFICATE OF TRANSMISSION/MAILING**

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.			
Typed or printed name	Ping Xiao		
Signature		Date	9/24/04

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Office Application of:	Tae-Wan Kim	Docket No.:	5199-14
Serial No.:	10/702,578	Examiner:	to be assigned
Filed:	November 5, 2003	Group Art Unit:	1632
Title:	<b>NOVEL MODULATORS OF AMYLOID-BETA PRODUCTION AND USES THEREOF</b>		

September 24, 2004

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**INFORMATION DISCLOSURE STATEMENT**  
**UNDER 37 CFR §1.97(b)**

**Sir:**

In accordance with the duty of disclosure under 37 CFR §1.56, applicant hereby notifies the U. S. Patent and Trademark Office of the following documents, which are listed on the attached PTO/SB/08B form. The examiner may deem these documents to be relevant to patentability of the claims of the above-identified application. Copies of the documents are enclosed for the examiner's convenience.

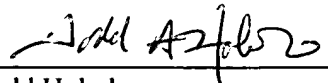
The submission of the listed documents is not intended as an admission that any of the documents constitute prior art against the claims of the present application. Applicants do not waive any right to take any action that would be appropriate to antedate or otherwise remove any listed document as a competent reference against the claims of the present application.

Applicants respectfully request that the listed documents be considered by the examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08B be returned in accordance with MPEP §609.

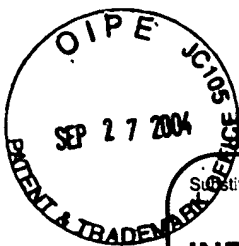
It is understood that no fee is necessary for submission of this Information Disclosure Statement, as it is being filed before the later of three months from the filing date or the mailing of the first Office Action on the merits.

The Commissioner is hereby authorized to charge payment of any fees associated with this application or credit any overpayment to Deposit Account No. 02-4270.

Respectfully submitted,

  
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Todd Holmbo  
Reg. No. 42,665  
Attorney for Applicants  
BROWN RAYSMAN MILLSTEIN  
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Substitute for form 1449/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

**Complete if Known**

Application Number	10/702,578
Filing Date	11/05/03
First Named Inventor	Tae-Wan Kim
Art Unit	1632
Examiner Name	to be assigned
Attorney Docket Number	5199-14

Sheet	1	of	10
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**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		Annaert et al., Interaction with telencephalin and the amyloid precursor protein predicts a ring structure for presenilins.	
		Neuron, 32: 579-89, 2001	
		Armogida et al., Endogenous beta-amyloid production in presenilin-deficient embryonic mouse fibroblasts.	
		Nat. Cell Biol., 3:1030-33, 2001	
		Ausubel et al., Current Protocols in Molecular Biology, New York: John Wiley and Sons, New York, 1997 (N/A)	
		Caplen et al., dsRNA-mediated gene silencing in cultured Drosophila cells: a tissue culture model for the analysis of RNA interference.	
		Gene, 252:95-105, 2000	
		Chen et al., Nicastrin binds to membrane-tethered Notch.	
		Nat. Cell Biol., 3:751-54, 2001	

Examiner Signature	Date Considered
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\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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	<b>First Named Inventor</b>		Tae-Wan Kim
	<b>Art Unit</b>		1632
	<b>Examiner Name</b>		to be assigned
	<b>Attorney Docket Number</b>		5199-14

Sheet

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of

10

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		Chung and Struhl, Nicastrin is required for Presenilin-mediated transmembrane cleavage in Drosophila.	
		Nature Cell Biol., 3:1129-32, 2001	
		Cupers et al., The discrepancy between presenilin subcellular localization and gamma-secretase processing of amyloid precursor protein.	
		J. Cell Biol., 154:731-40, 2001	
		De Strooper et al., Deficiency of presenilin-1 inhibits the normal cleavage of amyloid precursor protein.	
		Nature, 391:387-90, 1998	
		De Strooper and Annaert, Presenilins and the intramembrane proteolysis of proteins: facts and fiction.	
		Nat. Cell Biol., 3:E221-25, 2001	
		Ebinu and Yankner, A rip tide in neuronal signal transduction.	
		Neuron, 34:499-502, 2002	

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		First Named Inventor	Tae-Wan Kim
		Art Unit	1632
		Examiner Name	to be assigned
Sheet 3	of 10	Attorney Docket Number 5199-14	

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		Elbashir et al., Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells.	
		Nature, 411: 494-98, 2001	
		Elbashir et al., Functional anatomy of siRNAs for mediating efficient RNAi in Drosophila melanogaster embryo lysate.	
		EMBO J., 20:6877-88, 2001	
		Elbashir et al., RNA interference is mediated by 21- and 22- nucleotide RNAs.	
		Genes Dev., 15:188-200, 2001	
		Esler et al., Activity-dependent isolation of the presenilin gamma-secretase complex reveals nicastrin and a gamma substrate.	
		Proc. Natl. Acad. Sci. USA, 99:2720-25, 2002	
		Esler et al., Transition-state analogue inhibitors of gamma-secretase bind directly to presenilin-1.	
		Nature Cell Biol., 2:428, 2000	

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Sheet 4	of 10	Attorney Docket Number 5199-14	

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		Fire, A. RNA-triggered gene silencing.	
		Trends Genet., 15:358-63, 1999	
		Francis et al., Neuregulins and ErbB receptors in cultured neonatal astrocytes.	
		J. Neurosci. Res., 57:487-94, 1999	
		Goutte et al., APH-1 is a multipass membrane protein essential for the Notch signaling pathway in Caenorhabditis elegans embryos.	
		Proc. Natl. Acad. Sci, USA, 99:775-79, 2002	
		Hammond et al., An RNA-directed nuclease mediates post-transcriptional gene silencing in Drosophila cells.	
		Nature, 404:293-96, 2000	
		Hardy, J., Amyloid, the presenilins and Alzheimer's disease.	
		Trends Neurosci., 20:154-59, 1997	

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Sheet	5	of	10	Attorney Docket Number	5199-14

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		Hu and Fortini, Nicastrin is required for gamma-secretase cleavage of the Drosophila Notch receptor.	
		Dev. Cell, 2:69-78, 2002	
		Kehoe et al., A full genome scan for late onset Alzheimer's disease.	
		Hum. Mol. Genet., 8:237-45, 1999	
		Kim et al., Endoproteolytic cleavage and proteasomal degradation of presenilin 2 in transfected cells.	
		J. Biol. Chem., 272:11006-010, 1997	
		Levitan and Greenwald, Facilitation of lin-12-mediated signaling by sel-12, a Caenorhabditis elegans S182 Alzheimer's disease gene.	
		Nature, 377:351-54, 1999	

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		L' Hernault and Arduengo, Mutation of a putative sperm membrane protein in Caenorhabditis elegans prevents sperm differentiation but not	
		its associated meiotic divisions.	
		J. Cell. Biol., 119:55-58, 1992	
		Li and Greenwald, HOP-1, a Caenorhabditis elegans presenilin, appears to be functionally redundant with SEL-12 presenilin and to facilitate LIN-12	
		and GLP-1 signaling.	
		Proc. Natl. Acad. Sci. USA, 94:12204-209, 1997	
		Li, et al., Presenilin 1 is linked with gamma-secretase activity in the detergent solubilized state.	
		Proc. Natl. Acad. Sci. USA, 97:6138-43, 2000	
		Li, et al., Photoactivated gamma-secretase inhibitors directed to the active site covalently label presenilin 1.	
		Nature, 405:689-94, 2000	

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		Dev. Cell, 2:79-89, 2002	
		Myers et al., Full genome screen for Alzheimer disease: Stage II analysis.	
		Am. J. Med. Genet., 114:235-44, 2002	
		Naruse et al., Effects of PS1 deficiency on membrane protein trafficking in neurons.	
		Neuron, 21:1213-21, 1998	
		Seiffert et al., Presenilin-1 and -2 are molecular targets for gamma-secretase inhibitors.	
		J. Biol. Chem., 275:34086-091, 2000	
		Selkoe, D.J., Alzheimer's disease: gene, proteins, and therapy.	
		Physiol. Rev., 81:741-66, 2001	

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		Sisodia and George-Hyslop, gamma-Secretase, Notch, alpha-beta and Alzheimer's disease: where do the presenilins fit in?	
		Nat. Rev. Neurosci., 3:281-90, 2002	
		Steiner and Haass, Intramembrane proteolysis by presenilins.	
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\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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		Filing Date	11/05/03
		First Named Inventor	Tae-Wan Kim
		Art Unit	1632
		Examiner Name	to be assigned
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		Thinakaran et al., Evidence that levels of presenilins (PS1 and PS2) are coordinately regulated by competition for limiting cellular factors.	
		J. Biol. Chem., 272:28415-422, 1997	
		Tomita et al., The first proline of PALP motif at the C terminus of presenilins is obligatory for stabilization, complex formation, and gamma-	
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		Cell, 107(2):173-82, 2001	
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		Sci. STKE, 95:PL1, 2001	

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		Yu et al., Nicastrin modulates presenilin-mediated notch / glp-1 signal transduction and betaAPP processing.	
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		Genomics, 50:121-28, 1998	

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